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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
AKHAVAN, RAMIN	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 09/22/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Applicant 09/20/04

Office Action Summary	Application No.	Applicant(s)	
	10/058,291	HARTLEY ET AL.	
	Examiner	Art Unit	
	Ramin (Ray) Akhavan	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 June 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *35,36,38-66,69-75 and 79-112* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *35-36, 38-66, 69-75 and 79-112* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Acknowledgment is made of an amendment/response, filed 06/24/2004, canceling claims 37, 67, 68, 76, and 78, and amending claims 35, 38-41, 52, 69 and 72. In addition, Applicants present new claims 101-112. Therefore, claims 35-36, 38-66, 69-75 and 79-112 are currently pending and under consideration in this action. All objections/rejections not repeated herein are hereby withdrawn. Where applicable, a response to Applicant's arguments will be included in the body of objections/rejections maintained. As any new grounds of rejection set forth are necessitated by material amendment to the claims, this **ACTION IS FINAL.**

Response to Amendment

The limitation, "immediately adjacent" (all independent claims) is considered a material change to the invention and is further considered new matter, as there is no literal support in the disclosure for this limitation. (See infra, 35 U.S.C. § 112, ¶ 1 Rejection; Rejection No. 3).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

1. Claims 52-68, 87-91 and 101-106 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement.

Applicants' assertion that the specification provides sufficient basis for the ordinary skilled artisan to envision embodiments of the claimed invention is not deemed persuasive. A

response to Applicants' arguments is included below. (Infra, Response to Arguments). The claims contain subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

The broadest claim is drawn to a nucleic acid comprising a functional antibiotic resistance gene, where *any* recombination site separates a first and second portion of the antibiotic resistance gene. The recombination site can reasonably be interpreted to comprise *any* site from *any* source and be of *any* type. Notwithstanding the separation of the two portions by a recombination site, the nucleic acid comprises a functional antibiotic resistance gene. Even in the most specific embodiments, the first portion of the antibiotic resistance gene is a promoter sequence and the recombination site is a lox or att site or mutants thereof. Therefore a recombination sequence comprising some sequence from lox or att (e.g. mutant) would satisfy the claim limitation.

Additionally, the lox site can be a loxP site. A reasonable interpretation of the term "loxP" is that it can be read broadly to encompass any functional variant of loxP that can be specifically recombined by the Cre recombinase (e.g. having the requisite Cre binding site). Therefore, the rejected claims encompass an enormous genus of nucleic acids that comprise a functional antibiotic resistance gene, notwithstanding the intervening recombination site sequences. The written description requirement for a claimed genus may be satisfied by sufficient description of a representative number of species by actual reduction to practice, reduction to drawings or by disclosure relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with a known or

disclosed correlation between function and structure or by a combination of such identifying characteristics sufficient to show applicant was in possession of the claimed genus.

The teachings of the specification appear to be limited to site-specific recombination sites utilized in a technique for recombination cloning wherein the first portion of antibiotic resistance gene (e.g. Kanamycin; "Km") comprises a regulatory sequence (e.g. repressor-specific binding site) and the second portion is the Km gene, each separated from the other by a site-specific recombination site, so that when the repressor binding site and repressor are present, then cells containing the Km gene remain sensitive to the antibiotic. (Spec. p. 44, Example 5). The specification does not provide a basis for the skilled artisan to envision other embodiments of the claimed invention wherein the nucleic acid encoding a functional antibiotic resistance gene, comprises a first portion and second portion separated by *any* recombination site sequence. For example, most of the rejected claims encompass embodiments where the nucleic acid simultaneously comprises a site-specific recombination site (e.g. LoxP) inserted into a protein coding sequence such that the nucleic acid encodes a functional protein and is capable of site-specific recombination.

Given the enormous breadth of the nucleic acids encompassed by the rejected claims, and given the limited description from the instant specification of such nucleic acids, the skilled artisan would not have been able to envision a sufficient number of specific embodiments to describe the broadly claimed genus of nucleic acids. Moreover, an applicant claiming a biotechnological invention cannot necessarily claim a genus after only describing a limited number of species, because there may be unpredictability in the results obtained from other

species. Therefore, the skilled artisan would reasonably have concluded that applicants were not in possession of the claimed invention.

Response to Arguments

Applicants assert that the Examiner has provided no evidence that the various recombination sites discussed in the specification for the recombination sites utilized in the Examples would in any way alter or preclude the practice of the presently claimed invention. (Remarks, p. 17, ¶ 1). Applicants are reminded that this assertion is relevant to an enablement rejection not a written description rejection. Furthermore, in essence Applicants are arguing limitations, which are not claimed, because the examples/discussion in the specification are directed to site-specific recombination, but the claims are broadly drawn to any recombination site. (e.g. Spec. p. 14, ll. 1-15; p. 17, ll. 1-12; pp. 22-30). In addition, as pointed out previously, a reasonable interpretation of claims is that one of skill would have to envision any functional variant of the particular site-specific recombination sites disclosed. Applicants do not set forth how disclosure of a single embodiment (i.e. loxP) would sufficiently describe a sufficient number of embodiments. Moreover, as pointed out previously, the claims are also directed to vast number of embodiments directed to sequences that comprise a functional antibiotic resistance gene. Applicants do not present any arguments how the limited disclosure of certain antibiotic resistance genes would sufficiently apprise one of skill of the structure for all the claimed embodiments. The rejected claims encompass an enormous genus of nucleic acid molecules that comprise a functional antibiotic resistance gene, in addition to the genus of intervening recombination site sequences. Applicants have not presented any other arguments as

to how the specification sufficiently identifies the vast breadth of nucleic acid molecules for the claimed invention. Therefore, this rejection is maintained.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claim 39-66, 79-96 and 101-106 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Applicants' assertion that the terms, "recombination site" and "cloning site" are not vague and indefinite is not deemed persuasive. (See infra, Response to Arguments, immediately following the body of this rejection). Claim 39, 43-45, 52, 55-56 and 58-60 recite the limitation "recombination site". The term does not appear to be explicitly defined in the instant specification. This term is vague and indefinite in that it is unclear if the term is meant to encompass literally any nucleic acid that might serve as a site for a recombination (e.g. homologous, non-homologous recombination, etc.) or is meant, as appears to be the case upon reading the specification, a site-specific recombination sequence? Dependant claims drawn to nucleic acids *comprising* site-specific sequences (e.g. loxP) remain vague and indefinite, because such nucleic acids may contain sequences at the recombination site in addition to the site-specific sequence.

Claim 47 and 62 recite the limitation "one cloning site". The term does not appear to be explicitly defined in the instant specification. The term is vague and indefinite in that it is

unclear what the term encompasses. Does applicant intend that the term be drawn to recombination sites or restriction enzyme sites?

Response to Arguments

Applicants submit that one of ordinary skill in the art would readily understand that "recombination site" refers to a site-specific recombination site. (Remarks, pp. 19-20). This assertion is not deemed persuasive. Applicants point out to various portions of the specification that discuss or describe *site-specific recombination*. This limitation is simply not being claimed and as a term of art, "recombination site" does not automatically signal to one of ordinary skill in the art that the particular site is involved in site-specific recombination. Applicants are required to particularly point out and distinctly claim their invention. That Applicants are pointing out discussion/examples in the specification which all point to site-specific recombination, in and of itself, supports the fact that the claims as written, reciting "recombination site", are vague and indefinite. (e.g. Spec. p. 17, ll. 1-10; p. 18, ll. 19-20; pp. 24-26).

With respect to the term, "cloning site" being vague and indefinite, Applicants submit in referring to Figure 3D and the corresponding description in the specification, that two site-specific recombination sites flank a multiple cloning site. (Remarks, p. 21, last ¶, bridging to p. 22). Therefore, Applicants indicate the term, "cloning site", is sufficiently defined and would readily be understood. If the limitation – multiple cloning site – is what was intended, then it would have been remedial to substitute the term, "multiple cloning site" (MPS), instead of the ambiguous term, "cloning site". MPS would readily be understood by one of ordinary skill in the art. However, where the claims recite cloning site, but the specification discloses "multiple

cloning site", there is ambiguity, thus making the claims' metes and bounds indefinite. This rejection is maintained.

3. Claims 35-36, 38-66, 69-75 and 79-112 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement.

This is a new ground of rejection necessitated by material amendments to the claims. The claims contain subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. More particularly, all independent claims recite the limitation, "immediately adjacent", which does not have literal support in the specification. Applicants point to several different passages in the specification, however none of these passages or any other passages appear to contain support for said limitation. Therefore, the **limitation, "immediately adjacent" is deemed NEW MATTER**.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after

the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ray Akhavan whose telephone number is 571-272-0766. The examiner can normally be reached between 8:30-5:00, Monday-Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, PhD, can be reached on 571-272-0781. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Respectfully submitted,

Ray Akhavan/AU 1636

GERRY LEFFERS
PRIMARY EXAMINER